REMARKS

Prior to amendment, Claims 1-7, 9-13, 15, 16 and 18-43 were present in the application and stand rejected. By the foregoing amendments, the limitation of original Claim 12 (the concentration of the chelating agent is between about 5 mM and about 250 mM) has been incorporated into Claims 1, 23 and 40, and Claim 12 has been canceled. It is believed that amended Claims 1-7, 9-11, 13, 15, 16 and 18-43 are in condition for allowance in view of the following comments. A Request for Continued Examination (RCE) is submitted herewith. Reconsideration and favorable action is requested.

In the Advisory Action, the Examiner has stated that, "The claims recite components present in concentrations 'from about 1-20% [sic] and from about 1-250 mM for the surfactant and chelating agent respectively. These ranges though not expressly disclosed in the prior art are wide enough to encompass the concentrations disclosed." As set forth above, the independent claims have been amended to require that the chelating agent be present in an amount of about 5 mM to about 250 mM. Mulder U.S. Patent No. 5,565,189 (the Mulder '189 patent) discloses compositions including EDTA to prevent microbial growth during storage at a concentration of 0.08-0.12 wt %. This corresponds to an EDTA concentration of about 2.1 to 3.2 mM. Accordingly, the amount of EDTA in the compositions of the Mulder '189 patent fall substantially below the amounts claimed in the present application, where EDTA plays an active role in synergistically cooperating with cocamidopropyl betaine to enhance antimicrobial activity of the skin cleanser.

Rejections Under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1-7, 9, 11-13, 15, 16, 18, 19 and 23-39 under 35 U.S.C. § 103(a) as being unpatentable over Mulder U.S. Patent No. 5,565,189 (the Mulder '189 patent) in view of both Steel et al. U.S. Patent No. 6,224,853 (the Steel et al. '853 patent)

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and Huber et al. U.S. Patent No. 3,758,682 (the Huber et al. '682 patent). As set forth above, Claim 12 has been canceled.

The Examiner has cited the Mulder '189 patent as disclosing a method of cleaning the skin comprising the application of a cleansing composition comprising a carrier, water and aloe vera gel, a pH buffer such as sodium borate, chelators such as EDTA, vitamin E surfactants such as cocamphoacetate, and biocides such as hydroxyquinoline (citing example 1). The method further debriding the wound site, rinsing the composition after it is applied (citing Column 4, lines 45-55). The pH of the composition is between pH 6.5-6.8 (Column 4, lines 3-10). The formulation includes sensitizers that relieve pain (example 1).

The Examiner has indicated that the Mulder '189 patent does not disclose the specific compounds of the instant claims, but that these compounds are well known and their inclusion is within the level of skill in the art as shown by the Steel et al. '853 patent and the Huber et al. '682 patent.

The Examiner has cited the Steel et al. '853 patent as disclosing an aqueous formulation comprising lanolin and further cosurfactants such as cocamidopropyl betaine and lecithin where the surfactant is present in a concentration from 1-25% (citing Column 4, lines 18-39, Column 5, lines 20-45; Column 6, lines 40-50). The Examiner has cited the Huber et al. '682 patent as disclosing a formulation useful in wound healing comprising a buffer solution comprising tris(hydroxymethyl) amino methane (citing Column 13; lines 25-30), and that the composition can be administered orally contacting the oral mucosa (citing Column 24, lines 19-53).

The Mulder '189 patent discloses a non-sensitizing, over-the-counter wound cleanser composed of a carrier portion (70-90 wt% of the cleanser; Column 2, lines 28-35), an emollient portion (up to 10 wt% of the cleanser; Column 2, lines 36-46), a humectant portion (up to 10 wt% of the cleanser; Column 2, lines 47-53), a surfactant portion (up to 10 wt% of the cleanser;

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Column 2, lines 54-60), a preservative portion (up to 1.5 wt% of the cleanser; Column 2, lines 54-60), and a cosmetic biocide (oxyquinoline, up to 2 wt% of the cleanser; Column 3, lines 3-4).

As described in the Mulder '189 patent, the preservative portion is employed in the disclosed cleanser only to prevent microbial growth during storage. It should be noted that EDTA is commonly employed in many food and drug products as an antimicrobial preservative (but not as an active, functional component as claimed in the present application). Accordingly, the preservative portion can be 0.08-0.12 wt % sodium EDTA and 0.7-1.2 wt % alkyl paraben (Column 2, lines 61-67). In the only disclosed example, disodium EDTA is employed at a concentration of only 0.1% (Table 1, Column 4, line 38). Thus, the Mulder '189 patent discloses the use of EDTA at relatively low levels (0.08-0.12 wt. %, corresponding to about 2.1 to about 3.2 mM) as a preservative only, and does not disclose or suggest that EDTA could or should be employed at higher levels (about 5 mM to about 250 mM) to act synergistically as an active and functional agent in a skin cleanser composition, as claimed in the present application. In addition, the pH of the cleanser of the Mulder '189 patent is maintained within the range of 6.5 to 6.8 by the addition of an alkalizer (up to 1% (wt/wt) triethanolamine or sodium borate or an acid/conjugate base buffering system, to maintain the pH of the cleanser within the range of 6.5 to 6.8 to assist in reepithelialization of a wound site (Column 4, lines 3-16).

As described in the present application, the compositions of the present claims comprise a chelating agent, such as EDTA, and a pH buffering agent, such as Tris, in amounts sufficient to act as active components in potentiating the antibacterial activity of the detergent, cocamidopropyl betaine, or an added antimicrobial agent. As described in the specification at page 6, lines 12-19, the detergent or antimicrobial agent(s) has increased antimicrobial activity because of the synergy with the chelating agent and maintenance of the treated area at a pH

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suitable for sustained antibiotic activity. The antimicrobial agent can, therefore, be used in effective doses that are less than would be required for the same level of antimicrobial activity in the absence of the chelator. The compositions of the invention are therefore useful in counteracting or preventing an infection and are effective against infections caused by drug-resistant strains of microbes. Thus, the present invention sharply contrasts with the disclosure of the Mulder '189 patent where EDTA is employed at low levels solely as a preservative to prevent microbial growth during storage and not as an active component of the composition. Presumably, EDTA as disclosed by Mulder '189 patent could be substituted by any of large number of non-chelating agent preservatives commonly employed in the food, beverage and cosmetic industries to prevent contamination during storage, none of which would act synergistically to enhance antimicrobial activity of the skin cleanser as claimed in the present application.

There is no disclosure or suggestion in the Mulder '189 patent of a composition comprising 5 mM to about 250 mM of a chelating agent, such as EDTA, and cocamidopropyl betaine in amounts sufficient to act as active components in potentiating the antibacterial activity of the skin cleanser at a pH in the range of 7.0 to 9.0, as in the present invention. Accordingly, the Mulder '189 patent contains no disclosure or suggestion of a skin cleanser comprising from about 5 mM to about 250 mM of a chelating agent, a pH buffer for maintaining the pH of the cleanser in the range of 7.0 to 9.0, and from about 1 to about 30% by volume of cocamidopropyl betaine, wherein the amounts of the chelating agent and the cocamidopropyl betaine relative to each other are selected to allow the chelating agent and the cocamidopropyl betaine to synergistically cooperate to enhance antimicrobial activity of the skin cleanser when in aqueous solution, as required by the claims of the present application. The invention of applicants' claims would not have been obvious to a person of ordinary skill in the art in view of this reference.

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The Steel et al. '853 patent discloses an aqueous emulsion composition useful as a carrier for transdermal delivery of pharmaceutical actives to the human skin comprising water and (a) one or more surfactant materials selected from polyoxyalkylene condensate derivatives of lanolin or a lanolin derivative and (b) a lipid component comprising one or more lipid materials present as particles having a median particle size of less than about 5μ, emulsified by the lanolin-derived surfactant materials. At Column 4, lines 40-49, the Steel et al. '853 patent discloses:

> The compositions of the invention may optionally additionally contain one or more co-surfactant materials, which may be selected from various natural, synthetic or semi-synthetic surface active substances capable of forming in the aqueous phase a matrix structure within which the other ingredients are dispersed. Such co-surfactants may serve as additional emulsifying agents for the lipid component and/or may be useful to adjust the overall physical properties of the compositions, e.g. in order to optionally suit particular end-uses. [Emphasis added.]

At Column 5, lines 29 and 30, the Steel et al. '853 patent discloses that a suitable co-surfactant (i.e., as an additional emulsifying agent) may be cocamidopropyl betaine. However, the Steel et al. '853 patent does not disclose or suggest a formulation comprising from 1-25% of cocamidopropyl betaine, as implied by the Examiner. Rather, the Steel et al. '853 patent discloses at Column 5, lines 40-44, that the total amount of surfactant (i.e., the amount of the primary surfactant, polyoxyalkylene condensate derivatives of lanoline or a lanolin derivative, plus the optional co-surfactant) is preferably in the range of 1-25% by weight. Accordingly, the Steel et al. '853 patent does not disclose or suggest a formulation comprising 1-25% of cocamidopropyl betaine; rather, this component, is present (if present at all) in undisclosed amounts as a co-surfactant in the formation of an emulsion. In addition, the Steel et al. '853 patent does not disclose or suggest a cleaner comprising from about 5 mM to about 250 mM of a chelating agent, a pH buffer for maintaining the pH of the cleanser in the range of 7.0 to 9.0, and from about 1 to about 30% by volume of cocamidopropyl betaine, or that the concentrations of the chelating agent and the cocamidopropyl betaine are selected to allow the chelating agent and

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the cocamidopropyl betaine to synergistically enhance the antimicrobial activity of the skin cleanser, as required by applicants' claims.

Although the Steel et al. '853 patent discloses cocamidopropyl betaine as an optional co-surfactant to lanolin-derived surfactant materials in the preparation of a microemulsion for use as a carrier of active pharmaceuticals in transdermal delivery of the pharmaceuticals, it does not overcome the deficiencies of the disclosure of the Mulder '189 patent, as discussed in detail above.

The Huber et al. '682 patent discloses pharmaceutical compositions comprising orgotein for ameliorating the adverse effects of inflammatory conditions, of stress conditions, including shock and toxemia, and of certain viral diseases. Although the Examiner has cited the Huber et al. '682 patent at Column 13, lines 25-30, as disclosing a formulation comprising tris(hydroxymethyl) amino methane as a buffer, it is respectfully submitted that the Examiner has misinterpreted this portion of the Huber et al. '682 patent. As disclosed at Column 12, line 64, through Column 13, line 34, the orgotein utilized in the composition is characterized by the isolation of orgotein from a mixture of proteins by a multiplicity of fractionation steps employing an aqueous solution at a pH of 1 to 13 in the presence of a salt of a divalent metal. The buffers disclosed are employed in the fractionation process to maintain the pH at the desired level. Accordingly, the Huber et al. '682 patent does not disclose or remotely suggest the use of tris(hydroxymethyl) amino methane in a cleanser comprising from about 5 mM to about 250 mM of a chelating agent, a pH buffer for maintaining the pH of the cleanser in the range of 7.0 to 9.0, and from about 1 to about 30% by volume of cocamidopropyl betaine, or that the concentrations of the chelating agent and the cocamidopropyl betaine are selected to allow the chelating agent and the cocamidopropyl betaine to synergistically enhance the antimicrobial activity of the skin cleanser, as required by applicants' amended claims, and does not overcome the deficiencies of

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the disclosure of the Mulder '189 patent or the Steel et al. '853 patent, as discussed in detail above.

For the foregoing reasons, Claims 1-7, 9, 11, 13, 15, 16, 18, 19 and 23-39 would not have been obvious under 35 U.S.C. §103(a) as being unpatentable over the Mulder '189 patent in view of the Steel et al. '853 patent and the Huber et al. '682 patent, and this rejection should properly be withdrawn.

The Examiner has further rejected Claims 1, 4, 10 and 20 under 35 U.S.C. § 103(a) as being unpatentable over the Mulder '189 patent in view of the Steel et al. '853 patent and Robertson et al. U.S. Patent No. 4,939,135 (the Robertson et al. '135 patent). The Examiner has relied on the Robertson et al. '135 patent as disclosing a wound healing formulation and method of applying the formulation to an ocular injury (citing the abstract), the formulation comprising anti-inflammatory agents such as dexamethasone and antimicrobials such as neomycin and vancomycin (citing Column 4, lines 60-68), with the active agents in a concentration from 0.5-1.0% of the total formulation (Column 8, lines 1-5), the formulation further comprising chelators and sorbic acid (citing Column 10, lines 60-65). The Examiner has concluded that an artisan of ordinary skill would be motivated to combine the components of the Mulder '189 patent with those of the Robertson et al. '135 patent since they both solve the same problem of wound management with cleansing compositions.

The deficiencies in the disclosures of the Mulder '189 patent and the Steel et al. '853 patent are discussed in detail above, and are fully applicable to this rejection.

The Robertson et al. '135 patent is directed to compositions and methods for the treatment of corneal haze resulting from photoblation of the cornea during ophthalmic surgery. Agents used in the compositions include steroids, growth factors, basement membrane components, anti-oxidants, regulators of collagen structure, aldose reductase inhibitors, nonsteroidal

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antiinflammatories, immunomodulators, antiallergics, fatty acid derivatives which are products of the arachidonic acid cascade and antimicrobials (see Column 3, lines 16-35). The Robertson et al. '135 patent discloses at Column 10, lines 54-64, which in addition to the principal active ingredients, the disclosed wound healing modulator compositions may optionally further comprise from about 0.0001 wt. % to 1.0 wt. % of various antimicrobial preservatives, such as EDTA. As discussed above in connection with the Mulder '189 patent, antimicrobial preservatives are employed at low levels (substantially below 5 mM) to prevent microbial growth during product storage. Accordingly, the Robertson et al. '135 patent does not disclose or suggest a cleanser formulation comprising a chelating agent, such as EDTA, and a pH buffering agent, such as Tris, in amounts sufficient to act as active components in potentiating the antibacterial activity of the detergent, cocamidopropyl betaine, or an added antimicrobial agent, as claimed in the present application.

The Robertson et al. '135 patent does not overcome the deficiencies of the disclosure of the Mulder '189 patent and the Steel et al. '853 patent, as discussed in detail above, and Claims 1, 4, 10 and 20 would not have been obvious under 35 U.S.C. § 103(a) over the Mulder '189 patent in view of Steel et al. '853 patent and the Robertson et al. '135 patent, and this rejection should properly be withdrawn.

The Examiner has further rejected Claims 1, 21 and 22 under 35 U.S.C. § 103(a) over the combined disclosures of the Mulder '189 patent in view of the Steel et al. '853 patent and Gehlsen U.S. Patent No. 6,270,781 (the Gehlsen '781 patent). Claims 21 and 22 relate to the skin cleanser of Claim 1 which further comprise a colorant or a perfume, respectively. The Examiner has cited the Gehlsen '781 patent as disclosing a topical skin composition comprising detergents, antimicrobial agents, perfumes and pigments (citing Column 8, lines 6-15; Column 8, lines 57-65; and Column 9, lines 28-32). It is the Examiner's position that an artisan of ordinary skill

would have been motivated to include the pigments and perfumes of the Gehlsen '781 patent with the formulation of the Mulder '189 patent since they comprise similar components in the same field of endeavor.

The deficiencies in the disclosures of the Mulder '189 patent and the Steel et al. '853 patent are discussed in detail above, and are fully applicable to this rejection.

The Gehlsen '781 patent discloses topical formulations containing compounds that reduce or inhibit the amount of reactive oxygen metabolites (ROMs) and secondary cytokines produced or released by sources within a subject to facilitate the treatment of individuals suffering from a variety of skin and mucosal conditions, such as herpes infections and photodermatitis. Although the Gehlsen '781 patent discloses that its compositions containing its ROM inhibitory compounds may contain colorants or perfumes, it does not disclose or suggest the skin cleansers of applicants' amended claims, and does nothing to overcome the deficiencies of the Mulder '189 patent and the Steel et al. '853 patent, discussed in detail above. Accordingly, Claims 1, 21 and 22 would not have been obvious under 35 U.S.C. § 103(a) over the Mulder '189 patent in view of the Steel et al. '853 patent and the Gehlsen '781 patent, and this rejection should properly be withdrawn.

Finally, the Examiner has additionally rejected Claims 40-43 under 35 U.S.C. § 103(a) as being unpatentable over the combined disclosures of the Mulder '189 patent in view of the Steel et al. '853 patent and Horn U.S. Patent No. 5,848,700 (the "Horn '700 patent"). Claims 40-43 relate to kits container the skin cleanser of applicants' amended claims. The Examiner has cited the Horn '700 patent as disclosing a kit comprising instructions for various applications methods including cleansing the skin of burns, cuts, wounds and fractures (claims). It is the Examiner's position that it would have been obvious to include the skin cleanser of the Mulder '189 patent

and the Steel et al. '853 patent with the instructions of the Horn '700 patent, since they both endeavor to treat wounds.

The deficiencies in the disclosures of the Mulder '189 patent and the Steel et al. '853 patent are discussed in detail above, and are fully applicable to this rejection.

The Horn '700 patent discloses an emergency medical care kit that comprises a carrying case approximately the size of a briefcase or small suitcase with the upper and lower sections divided into a large number of compartments by insertion of a plastic organizer with removable covers. The reverse side of each compartment cover has instructions for treating the particular emergency, while the compartment itself contains the necessary care items for that particular emergency. A hinged divider is held by snaps across the upper section of the case to help contain the contents and also provides instruction for use of the kit, some general first aid information, and a list of emergency telephone numbers.

Although the Horn '700 patent discloses a kit for medical emergencies, it does not disclose or remotely suggest the skin cleansers of applicants' claims, and does not overcome the deficiencies of the Mulder '189 patent and the Steel et al. '853 patent, discussed in detail above. Accordingly, Claims 40-43 would not have been obvious under 35 U.S.C. § 103(a) over the Mulder '189 patent in view of the Horn '700 patent.

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Conclusion

In view of the foregoing amendments and comments, Claims 1-7, 9-11, 13, 15, 16, and 18-43 are believed to be in condition for allowance. Reconsideration and favorable action are requested. The Examiner is further requested to contact the applicants' representative by telephone to discuss any issues that may facilitate prosecution of the application.

Respectfully submitted,

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